

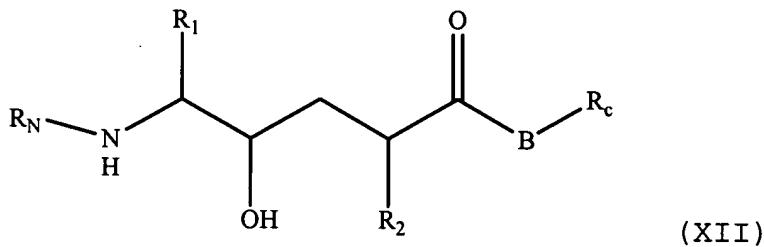
Response to April 12, 2005, Office Action  
Serial No.: 09/816,876  
Filed: March 23, 2001

Listing of Claims

This listing of claims will replace all prior versions and listings of claims in the application.

Claims 1-48. (Canceled)

Claim 49. (currently amended) A method for treating Alzheimer's disease ~~a disease characterized by beta amyloid deposits in the brain~~ comprising administering to a patient an effective therapeutic amount of a ~~hydroxyethylene~~ compound of the formula



where  $R_1$  is:

- (I)  $C_1-C_6$  alkyl, unsubstituted or substituted with one, two or three  $C_1-C_3$  alkyl,  $-F$ ,  $-Cl$ ,  $-Br$ ,  $-I$ ,  $-OH$ ,  $-NH_2$ ,  $-C\equiv N$ ,  $-CF_3$ , or  $-N_3$ ,
- (II)  $-(CH_2)_{1-2}-S-CH_3$ ,
- (III)  $-CH_2-CH_2-S-CH_3$ ,
- (IV)  $-CH_2-(C_2-C_6$  alkenyl) unsubstituted or substituted by one  $-F$ ,
- (V)  $-(CH_2)_{0-3}-(R_1-aryl)$  where  $R_1-aryl$  is phenyl, 1-naphthyl, 2-naphthyl, indanyl, indenyl, dihydronaphthyl, tetralinyl unsubstituted or substituted on the aryl ring with one or two of

the following substituents which can be the same or different:

- (A) C<sub>1</sub>-C<sub>3</sub> alkyl,
- (B) -CF<sub>3</sub>,
- (C) -F, Cl, -Br and -I,
- (D) C<sub>1</sub>-C<sub>3</sub> alkoxy,
- (E) -O-CF<sub>3</sub>,
- (F) -NH<sub>2</sub>,
- (G) -OH, or
- (H) -C≡N,

(VI) -(CH<sub>2</sub>)<sub>n1</sub>-(R<sub>1</sub>-heteroaryl) where n<sub>1</sub> is 0, 1, 2, or 3 and R<sub>1</sub>-heteroaryl is:

- (A) pyridinyl,
- (B) pyrimidinyl,
- (C) quinolinyl,
- (D) indenyl,
- (E) indanyl,
- (F) benzothiophenyl,
- (G) indolyl,
- (H) indolinyl,
- (I) pyridazinyl,
- (J) pyrazinyl,
- (K) isoindolyl,
- (L) isoquinolyl,
- (M) quinazolinyl,
- (N) quinoxalinyl,
- (O) phthalazinyl,
- (P) imidazolyl,
- (Q) isoxazolyl,
- (R) pyrazolyl,
- (S) oxazolyl,

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- (T) thiazolyl,
- (U) indolizinyl,
- (V) indazolyl,
- (W) benzothiazolyl,
- (X) benzimidazolyl,
- (Y) benzofuranyl,
- (Z) furanyl,
- (AA) thiaryl,
- (BB) pyrrolyl,
- (CC) oxadiazolyl,
- (DD) thiadiazolyl,
- (EE) triazolyl,
- (FF) tetrazolyl,
- (GG) 1, 4-benzodioxan
- (HH) purinyl,
- (II) oxazolopyridinyl,
- (JJ) imidazopyridinyl,
- (KK) isothiazolyl,
- (LL) naphthyridinyl,
- (MM) cinnolinyl,
- (NN) carbazolyl,
- (OO)  $\beta$ -carbolinyl,
- (PP) isochromanyl,
- (QQ) chromanyl,
- (RR) furazanyl,
- (SS) tetrahydroisoquinoline,
- (TT) isoindolinyl,
- (UU) isobenzotetrahydrofuranyl,
- (VV) isobenzotetrahydrothienyl,
- (WW) isobenzothiophenyl,
- (XX) benzoxazolyl, or

(YY) pyridopyridinyl,

where the R<sub>1</sub>-heteroaryl group is bonded to -(CH<sub>2</sub>)<sub>0-3</sub>- by any ring atom of the parent R<sub>N</sub>-heteroaryl group substituted by hydrogen such that the new bond to the R<sub>1</sub>-heteroaryl group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

- (1) C<sub>1</sub>-C<sub>3</sub> alkyl,
- (2) -CF<sub>3</sub>,
- (3) -F, Cl, -Br, or -I,
- (4) C<sub>1</sub>-C<sub>3</sub> alkoxy,
- (5) -O-CF<sub>3</sub>,
- (6) -NH<sub>2</sub>,
- (7) -OH, or
- (8) -C≡N,

with the proviso that when n<sub>1</sub> is zero R<sub>1</sub>-heteroaryl is not bonded to the carbon chain by nitrogen, or

(VII) -(CH<sub>2</sub>)<sub>n1</sub>-(R<sub>1</sub>-heterocycle) where n<sub>1</sub> is as defined above and

R<sub>1</sub>-heterocycle is:

- (A) morpholinyl,
- (B) thiomorpholinyl,
- (C) thiomorpholinyl S-oxide,
- (D) thiomorpholinyl S,S-dioxide,
- (E) piperazinyl,
- (F) homopiperazinyl,
- (G) pyrrolidinyl,
- (H) pyrrolinyl,
- (I) tetrahydropyranyl,
- (J) piperidinyl,
- (K) tetrahydrofuranyl, or
- (L) tetrahydrothiophenyl,

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where the R<sub>1</sub>-heterocycle group is bonded by any atom of the parent R<sub>1</sub>-heterocycle group substituted by hydrogen such that the new bond to the R<sub>1</sub>-heteroaryl group replaces the hydrogen atom and its bond, where heterocycle is unsubstituted or substituted with one or two:

- (1) =O,
- (2) C<sub>1</sub>-C<sub>3</sub> alkyl,
- (3) -CF<sub>3</sub>,
- (4) -F, Cl, -Br and -I,
- (5) C<sub>1</sub>-C<sub>3</sub> alkoxy,
- (6) -O-CF<sub>3</sub>,
- (7) -NH<sub>2</sub>,
- (8) -OH, or
- (9) -C≡N,

with the proviso that when n<sub>1</sub> is zero R<sub>1</sub>-heterocycle is not bonded to the carbon chain by nitrogen;

where R<sub>2</sub> is:

- (I) -H,
- (II) C<sub>1</sub>-C<sub>6</sub> alkyl, or
- (III) -(CH<sub>2</sub>)<sub>0-4</sub>-R<sub>2-1</sub> where R<sub>2-1</sub> is (C<sub>3</sub>-C<sub>6</sub>)cycloalkyl, R<sub>1</sub>-aryl or R<sub>1</sub>-heteroaryl where R<sub>1</sub>-aryl and R<sub>1</sub>-heteroaryl are as defined above,

where R<sub>N</sub> is:

- (I) R<sub>N-1</sub>-X<sub>N</sub>- where X<sub>N</sub> is:
  - (A) -CO-,
  - (B) -SO<sub>2</sub>-,
  - (C) -(CR'R")<sub>1-6</sub> where R' and R" are the same or different and are -H or C<sub>1</sub>-C<sub>4</sub> alkyl,
  - (D) -CO-(CR'R")<sub>1-6</sub>-X<sub>N-1</sub> where X<sub>N-1</sub> is -O-, -S- and -NR'R"- and where R' and R" are as defined above,

(E) a single bond;

where  $R_{N-1}$  is:

(A)  $R_N$ -aryl where  $R_N$ -aryl is phenyl, 1-naphthyl and 2-naphthyl unsubstituted or substituted with one, two, three or four of the following substituents which can be the same or different and are:

- (1)  $C_1-C_6$  alkyl,
- (2) -F, -Cl, -Br, or -I,
- (3) -OH,
- (4) -NO<sub>2</sub>,
- (5) -CO-OH,
- (6) -C≡N,
- (7) -CO-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are:

- (a) -H,
- (b)  $-C_1-C_6$  alkyl unsubstituted or substituted with one
  - (i) -OH, or
  - (ii) -NH<sub>2</sub>,
- (c)  $-C_1-C_6$  alkyl unsubstituted or substituted with one to three -F, -Cl, -Br, or -I,
- (d) -C<sub>3</sub>-C<sub>7</sub> cycloalkyl,
- (e) -(C<sub>1</sub>-C<sub>2</sub> alkyl)-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl),
- (f) -(C<sub>1</sub>-C<sub>6</sub> alkyl)-O-(C<sub>1</sub>-C<sub>3</sub> alkyl),
- (g) -C<sub>1</sub>-C<sub>6</sub> alkenyl with one or two

double bonds,

(h) -C<sub>1</sub>-C<sub>6</sub> alkynyl with one or two triple bonds,

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- (i) -C<sub>1</sub>-C<sub>6</sub> alkyl chain with one double bond and one triple bond,
- (j) -R<sub>1</sub>-aryl where R<sub>1</sub>-aryl is as defined above, or
- (k) -R<sub>1</sub>-heteroaryl where R<sub>1</sub>-heteroaryl is as defined above,
- (8) -CO- (C<sub>3</sub>-C<sub>12</sub> alkyl),
- (9) -CO- (C<sub>3</sub>-C<sub>6</sub> cycloalkyl),
- (10) -CO-R<sub>1</sub>-heteroaryl where R<sub>1</sub>-heteroaryl is as defined above,
- (11) -CO-R<sub>1</sub>-heterocycle where R<sub>1</sub>-heterocycle is as defined above,
- (12) -CO-R<sub>N-4</sub> where R<sub>N-4</sub> is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two C<sub>1</sub>-C<sub>3</sub> alkyl,
- (13) -CO-O-R<sub>N-5</sub> where R<sub>N-5</sub> is:
  - (a) C<sub>1</sub>-C<sub>6</sub> alkyl, or
  - (b) -(CH<sub>2</sub>)<sub>0-2-</sub>(R<sub>1</sub>-aryl) where R<sub>1</sub>-aryl is as defined above,
- (14) -SO<sub>2</sub>-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are as defined above,
- (15) -SO-(C<sub>1</sub>-C<sub>8</sub> alkyl),
- (16) -SO<sub>2</sub>-(C<sub>3</sub>-C<sub>12</sub> alkyl),
- (17) -NH-CO-O-R<sub>N-5</sub> where R<sub>N-5</sub> is as defined above,
- (18) -NH-CO-N(C<sub>1</sub>-C<sub>3</sub> alkyl)<sub>2</sub>,
- (19) -N-CS-N(C<sub>1</sub>-C<sub>3</sub> alkyl)<sub>2</sub>,
- (20) -N(C<sub>1</sub>-C<sub>3</sub> alkyl)-CO-R<sub>N-5</sub> where R<sub>N-5</sub> is as defined above,

(21)  $-NR_{N-2}R_{N-3}$  where  $R_{N-2}$  and  $R_{N-3}$  can be the same or different and are as defined above,

(22)  $-R_{N-4}$  where  $R_{N-4}$  is as defined above,

(23)  $-O-CO-(C_1-C_6\text{ alkyl})$ ,

(24)  $-O-CO-N(C_1-C_3\text{ alkyl})_2$ ,

(25)  $-O-CS-N(C_1-C_3\text{ alkyl})_2$ ,

(26)  $-O-(C_1-C_6\text{ alkyl})$ ,

(27)  $-O-(C_2-C_5\text{ alkyl})-COOH$ ,

(28)  $-S-(C_1-C_6\text{ alkyl})$ ,

(29)  $C_1-C_6$  alkyl unsubstituted or substituted with 1, 2, 3, 4, or 5 -F,

(30)  $-O-(C_1-C_6\text{ alkyl})$  unsubstituted or substituted with 1, 2, 3, 4, or 5 -F, or

(31)  $-O-\phi$ ,

(B)  $-R_N\text{-heteroaryl}$  where  $R_N\text{-heteroaryl}$  is:

- (A) pyridinyl,
- (B) pyrimidinyl,
- (C) quinolinyl,
- (D) indenyl,
- (E) indanyl,
- (F) benzothiophenyl,
- (G) indolyl,
- (H) indolinyl,
- (I) pyridazinyl,
- (J) pyrazinyl,
- (K) isoindolyl,
- (L) isoquinolyl,
- (M) quinazolinyl,
- (N) quinoxalinyl,
- (O) phthalazinyl,

- (P) imidazolyl,
- (Q) isoxazolyl,
- (R) pyrazolyl,
- (S) oxazolyl,
- (T) thiazolyl,
- (U) indolizinyl,
- (V) indazolyl,
- (W) benzothiazolyl,
- (X) benzimidazolyl,
- (Y) benzofuranyl,
- (Z) furanyl,
- (AA) thietyl,
- (BB) pyrrolyl,
- (CC) oxadiazolyl,
- (DD) thiadiazolyl,
- (EE) triazolyl,
- (FF) tetrazolyl,
- (GG) 1, 4-benzodioxan
- (HH) purinyl,
- (II) oxazolopyridinyl,
- (JJ) imidazopyridinyl,
- (KK) isothiazolyl,
- (LL) naphthyridinyl,
- (MM) cinnolinyl,
- (NN) carbazolyl,
- (OO)  $\beta$ -carbolinyl,
- (PP) isochromanyl,
- (QQ) chromanyl,
- (RR) furazanyl,
- (SS) tetrahydroisoquinoline,
- (TT) isoindolinyl,

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- (UU) isobenzotetrahydrofuranyl,
- (VV) isobenzotetrahydrothienyl,
- (WW) isobenzothiophenyl,
- (XX) benzoxazolyl, or
- (YY) pyridopyridinyl,

where the R<sub>N</sub>-heteroaryl group is bonded by any atom of the parent R<sub>N</sub>-heteroaryl group substituted by hydrogen such that the new bond to the R<sub>N</sub>-heteroaryl group replaces the hydrogen atom and its bond, where heteroaryl is unsubstituted or substituted with one or two:

- (1) C<sub>1</sub>-C<sub>6</sub> alkyl,
- (2) -F, -Cl, -Br, or -I,
- (3) -OH,
- (4) -NO<sub>2</sub>,
- (5) -CO-OH,
- (6) -C≡N,
- (7) -CO-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are:
  - (a) -H,
  - (b) -C<sub>1</sub>-C<sub>6</sub> alkyl unsubstituted or substituted with one
    - (i) -OH, or
    - (ii) -NH<sub>2</sub>,
  - (c) -C<sub>1</sub>-C<sub>6</sub> alkyl unsubstituted or substituted with 1, 2, or 3 -F, -Cl, -Br, or -I,
  - (d) -C<sub>3</sub>-C<sub>7</sub> cycloalkyl,
  - (e) -(C<sub>1</sub>-C<sub>2</sub> alkyl)-(C<sub>3</sub>-C<sub>7</sub> cycloalkyl),
  - (f) -(C<sub>1</sub>-C<sub>6</sub> alkyl)-O-(C<sub>1</sub>-C<sub>3</sub> alkyl),

- (g) -C<sub>1</sub>-C<sub>6</sub> alkenyl with one or two double bonds,
- (h) -C<sub>1</sub>-C<sub>6</sub> alkynyl with one or two triple bonds,
- (i) -C<sub>1</sub>-C<sub>6</sub> alkyl chain with one double bond and one triple bond,
- (j) -R<sub>1</sub>-aryl where R<sub>1</sub>-aryl is as defined above, or
- (k) -R<sub>1</sub>-heteroaryl where R<sub>1</sub>-heteroaryl is as defined above,
- (8) -CO-(C<sub>3</sub>-C<sub>12</sub> alkyl),
- (9) -CO-(C<sub>3</sub>-C<sub>6</sub> cycloalkyl),
- (10) -CO-R<sub>1</sub>-heteroaryl where R<sub>1</sub>-heteroaryl is as defined above,
- (11) -CO-R<sub>1</sub>-heterocycle where R<sub>1</sub>-heterocycle is as defined above,
- (12) -CO-R<sub>N-4</sub> where R<sub>N-4</sub> is morpholinyl, thiomorpholinyl, piperazinyl, piperidinyl or pyrrolidinyl where each group is unsubstituted or substituted with one or two C<sub>1</sub>-C<sub>3</sub> alkyl,
- (13) -CO-O-R<sub>N-5</sub> where R<sub>N-5</sub> is:
  - (a) C<sub>1</sub>-C<sub>6</sub> alkyl, or
  - (b) -(CH<sub>2</sub>)<sub>0-2-</sub>(R<sub>1</sub>-aryl) where R<sub>1</sub>-aryl is as defined above,
- (14) -SO<sub>2</sub>-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are as defined above,
- (15) -SO-(C<sub>1</sub>-C<sub>8</sub> alkyl),
- (16) -SO<sub>2</sub>-(C<sub>3</sub>-C<sub>12</sub> alkyl),

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- (17) -NH-CO-O-R<sub>N-5</sub> where R<sub>N-5</sub> is as defined above,
- (18) -NH-CO-N(C<sub>1</sub>-C<sub>3</sub> alkyl)<sub>2</sub>,
- (19) -N-CS-N(C<sub>1</sub>-C<sub>3</sub> alkyl)<sub>2</sub>,
- (20) -N(C<sub>1</sub>-C<sub>3</sub> alkyl)-CO-R<sub>N-5</sub> where R<sub>N-5</sub> is as defined above,
- (21) -NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> can be the same or different and are as defined above,
- (22) -R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,
- (23) -O-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),
- (24) -O-CO-N(C<sub>1</sub>-C<sub>3</sub> alkyl)<sub>2</sub>,
- (25) -O-CS-N(C<sub>1</sub>-C<sub>3</sub> alkyl)<sub>2</sub>,
- (26) -O-(C<sub>1</sub>-C<sub>6</sub> alkyl),
- (27) -O-(C<sub>2</sub>-C<sub>5</sub> alkyl)-COOH, or
- (28) -S-(C<sub>1</sub>-C<sub>6</sub> alkyl),

(C) -R<sub>N-aryl</sub>-R<sub>N-aryl</sub> where -R<sub>N-aryl</sub> is as defined above,

(D) -R<sub>N-aryl</sub>-R<sub>N-heteroaryl</sub> where -R<sub>N-aryl</sub> and -R<sub>N-heteroaryl</sub> are as defined above,

(E) -R<sub>N-heteroaryl</sub>-R<sub>N-aryl</sub> where -R<sub>N-aryl</sub> and -R<sub>N-heteroaryl</sub> are as defined above,

(F) -R<sub>N-heteroaryl</sub>-R<sub>N-heteroaryl</sub> where R<sub>N-heteroaryl</sub> is as defined above,

(G) -R<sub>N-aryl</sub>-O-R<sub>N-aryl</sub> where -R<sub>N-aryl</sub> is as defined above,

(H) -R<sub>N-aryl</sub>-S-R<sub>N-aryl</sub> where -R<sub>N-aryl</sub> is as defined above,

(I) -R<sub>N-heteroaryl</sub>-O-R<sub>N-heteroaryl</sub> where R<sub>N-heteroaryl</sub> is as defined above,

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(J)  $-R_N\text{-heteroaryl-S-}R_N\text{-heteroaryl}$  where  $R_N\text{-heteroaryl}$  is as defined above,

(K)  $-R_N\text{-aryl-CO-}R_N\text{-aryl}$  where  $-R_N\text{-aryl}$  is as defined above,

(L)  $-R_N\text{-aryl-CO-}R_N\text{-heteroaryl}$  where  $-R_N\text{-aryl}$  and  $R_N\text{-heteroaryl}$  are as defined above,

(M)  $-R_N\text{-aryl-SO}_2\text{-}R_N\text{-aryl}$  where  $-R_N\text{-aryl}$  is as defined above,

(N)  $-R_N\text{-heteroaryl-CO-}R_N\text{-heteroaryl}$  where  $R_N\text{-heteroaryl}$  is as defined above,

(O)  $-R_N\text{-heteroaryl-SO}_2\text{-}R_N\text{-heteroaryl}$  where  $R_N\text{-heteroaryl}$  is as defined above,

(P)  $-R_N\text{-aryl-O-}(C_1\text{-}C_8 \text{ alkyl})-\phi$  where  $R_N\text{-aryl}$  is as defined above,

(Q)  $-R_N\text{-aryl-S-}(C_1\text{-}C_8 \text{ alkyl})-\phi$  where  $R_N\text{-aryl}$  is as defined above,

(R)  $-R_N\text{-heteroaryl-O-}(C_1\text{-}C_8 \text{ alkyl})-\phi$  where  $R_N\text{-heteroaryl}$  is as defined above, or

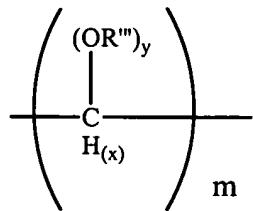
(S)  $-R_N\text{-heteroaryl-S-}(C_1\text{-}C_8 \text{ alkyl})-\phi$  where  $R_N\text{-heteroaryl}$  is as defined above,

(II)  $A-X_N-$  where  $X_N$  is  $-CO-,$

wherein A is

(A)  $-T-E-(Q)_m,$

(1) where  $-T$  is



where

(a) x = 1 when y = 1 and x = 2 when y = 0,

(b) m is 0, 1, 2 or 3,

(c) the values of x and y vary independently on each carbon when m is 2 and 3, and

(d) R''' varies independently on each carbon and is H, (C<sub>1</sub>-C<sub>2</sub>) alkyl, phenyl, or phenyl(C<sub>1</sub>-C<sub>3</sub>)alkyl;

(2) -E is

(a) C<sub>1</sub>-C<sub>5</sub> alkyl, but only if m' does not equal 0,

(b) methylthioxy(C<sub>2</sub>-C<sub>4</sub>)alkyl,

(c) an aryl group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,

(d) a heterocyclic group having 5 to 7 atoms when monocyclic or having 8 to 12 atoms when fused,

(e) a mono or fused ring cycloalkyl group having 5 to 10 carbon atoms,

(f) biphenyl,

(g) diphenyl ether,

(h) diphenylketone,

(i) phenyl(C<sub>1</sub>-C<sub>8</sub>)alkyloxyphenyl, or

(j) C<sub>1</sub>-C<sub>6</sub> alkoxy;

(3) -Q is

(a) C<sub>1</sub>-C<sub>3</sub> alkyl,

(b) C<sub>1</sub>-C<sub>3</sub> alkoxy,

(c) C<sub>1</sub>-C<sub>3</sub> alkylthioxy,

- (d) C<sub>1</sub>-C<sub>6</sub> alkylacylamino,
- (e) C<sub>1</sub>-C<sub>6</sub> alkylacyloxy,
- (f) amido (including primary, C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl secondary and tertiary amino moieties),
- (g) C<sub>1</sub>-C<sub>6</sub> alkylamino
- (h) phenylamino,
- (i) carbamyl (including C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl amides and esters),
- (j) carboxyl (including C<sub>1</sub>-C<sub>6</sub> alkyl and phenyl esters),
- (k) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkoxy,
- (l) carboxy(C<sub>2</sub>-C<sub>5</sub>)alkylthioxy,
- (m) heterocyclylacyl,
- (n) heteroarylacyl, or
- (o) hydroxyl;

(4) m' is 0, 1, 2 or 3;

(B) -E(Q)<sub>m''</sub> wherein E and -Q are as defined as above and m'' is 0, 1, 2, or 3;

(C) -T-E wherein -E and -Q are as defined as above; or

(D) -E wherein -E is as defined as above;

(III) -CO-(C<sub>1</sub>-C<sub>6</sub> alkyl) where alkyl is unsubstituted or substituted with one or two:

- (A) -OH,
- (B) -C<sub>1</sub>-C<sub>6</sub> alkoxy,
- (C) -C<sub>1</sub>-C<sub>6</sub> thioalkoxy,
- (D) -CO-O-R<sub>N-8</sub> where R<sub>N-8</sub> is -H, C<sub>1</sub>-C<sub>6</sub> alkyl or - $\phi$ ,
- (E) -CO-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,
- (F) -CO-R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,

- (G)  $-\text{SO}_2-(\text{C}_1\text{-C}_8 \text{ alkyl})$ ,
- (H)  $-\text{SO}_2-\text{NR}_{\text{N}-2}\text{R}_{\text{N}-3}$  where  $\text{R}_{\text{N}-2}$  and  $\text{R}_{\text{N}-3}$  are the same or different and are as defined above,
- (I)  $-\text{NH-CO-(C}_1\text{-C}_6 \text{ alkyl)}$ ,
- (J)  $-\text{NH-CO-O-R}_{\text{N}-8}$  where  $\text{R}_{\text{N}-8}$  is as defined above,
- (K)  $-\text{NR}_{\text{N}-2}\text{R}_{\text{N}-3}$  where  $\text{R}_{\text{N}-2}$  and  $\text{R}_{\text{N}-3}$  are the same or different and are as defined above,
- (L)  $-\text{R}_{\text{N}-4}$  where  $\text{R}_{\text{N}-4}$  is as defined above,
- (M)  $-\text{O-CO-(C}_1\text{-C}_6 \text{ alkyl)}$ ,
- (N)  $-\text{O-CO-NR}_{\text{N}-8}\text{R}_{\text{N}-8}$  where the  $\text{R}_{\text{N}-8}$  is the same or different and are as defined above, or
- (O)  $-\text{O-(C}_1\text{-C}_5 \text{ alkyl)-COOH}$ ,
- (IV)  $-\text{CO-(C}_1\text{-C}_3 \text{ alkyl)-O-(C}_1\text{-C}_3 \text{ alkyl)}$  where alkyl is unsubstituted or substituted with one or two
  - (A)  $-\text{OH}$ ,
  - (B)  $-\text{C}_1\text{-C}_6 \text{ alkoxy}$ ,
  - (C)  $-\text{C}_1\text{-C}_6 \text{ thioalkoxy}$ ,
  - (D)  $-\text{CO-O-R}_{\text{N}-8}$  where  $\text{R}_{\text{N}-8}$  is  $-\text{H}$ ,  $\text{C}_1\text{-C}_6$  alkyl or  $-\phi$ ,
  - (E)  $-\text{CO-NR}_{\text{N}-2}\text{R}_{\text{N}-3}$  where  $\text{R}_{\text{N}-2}$  and  $\text{R}_{\text{N}-3}$  are the same or different and are as defined above,
  - (F)  $-\text{CO-R}_{\text{N}-4}$  where  $\text{R}_{\text{N}-4}$  is as defined above,
  - (G)  $-\text{SO}_2-(\text{C}_1\text{-C}_8 \text{ alkyl})$ ,
  - (H)  $-\text{SO}_2-\text{NR}_{\text{N}-2}\text{R}_{\text{N}-3}$  where  $\text{R}_{\text{N}-2}$  and  $\text{R}_{\text{N}-3}$  are the same or different and are as defined above,
  - (I)  $-\text{NH-CO-(C}_1\text{-C}_6 \text{ alkyl)}$ ,
  - (J)  $-\text{NH-CO-O-R}_{\text{N}-8}$  where  $\text{R}_{\text{N}-8}$  is as defined above,
  - (K)  $-\text{NR}_{\text{N}-2}\text{R}_{\text{N}-3}$  where  $\text{R}_{\text{N}-2}$  and  $\text{R}_{\text{N}-3}$  are the same or different and are as defined above,
  - (L)  $-\text{R}_{\text{N}-4}$  where  $\text{R}_{\text{N}-4}$  is as defined above,
  - (M)  $-\text{O-CO-(C}_1\text{-C}_6 \text{ alkyl)}$ ,

(N) -O-CO-NR<sub>N-8</sub>R<sub>N-8</sub> where the R<sub>N-8</sub> are the same or different and are as defined above, or

(O) -O-(C<sub>1</sub>-C<sub>5</sub> alkyl)-COOH,

(V) -CO-(C<sub>1</sub>-C<sub>3</sub> alkyl)-S-(C<sub>1</sub>-C<sub>3</sub> alkyl) where alkyl is unsubstituted or substituted with one or two

(A) -OH,

(B) -C<sub>1</sub>-C<sub>6</sub> alkoxy,

(C) -C<sub>1</sub>-C<sub>6</sub> thioalkoxy,

(D) -CO-O-R<sub>N-8</sub> where R<sub>N-8</sub> is -H, C<sub>1</sub>-C<sub>6</sub> alkyl or -Φ,

(E) -CO-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,

(F) -CO-R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,

(G) -SO<sub>2</sub>-(C<sub>1</sub>-C<sub>8</sub> alkyl),

(H) -SO<sub>2</sub>-NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,

(I) -NH-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),

(J) -NH-CO-O-R<sub>N-8</sub> where R<sub>N-8</sub> is as defined above,

(K) -NR<sub>N-2</sub>R<sub>N-3</sub> where R<sub>N-2</sub> and R<sub>N-3</sub> are the same or different and are as defined above,

(L) -R<sub>N-4</sub> where R<sub>N-4</sub> is as defined above,

(M) -O-CO-(C<sub>1</sub>-C<sub>6</sub> alkyl),

(N) -O-CO-NR<sub>N-8</sub>R<sub>N-8</sub> where the R<sub>N-8</sub> are the same or different and are as defined above, or

(O) -O-(C<sub>1</sub>-C<sub>5</sub> alkyl)-COOH,

(VI) -CO-CH(-(CH<sub>2</sub>)<sub>0-2</sub>-O-R<sub>N-10</sub>)-(CH<sub>2</sub>)<sub>0-2</sub>-R<sub>N-aryl</sub>/R<sub>N-heteroaryl</sub>) where R<sub>N-aryl</sub> and R<sub>N-heteroaryl</sub> are as defined above, where R<sub>N-10</sub> is:

(A) -H,

(B) C<sub>1</sub>-C<sub>6</sub> alkyl,

(C) C<sub>3</sub>-C<sub>7</sub> cycloalkyl,

(D) C<sub>2</sub>-C<sub>6</sub> alkenyl with one double bond,

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(E) C<sub>2</sub>-C<sub>6</sub> alkynyl with one triple bond,  
(F) R<sub>1</sub>-aryl where R<sub>1</sub>-aryl is as defined above, or  
(G) R<sub>N</sub>-heteroaryl where R<sub>N</sub>-heteroaryl is as defined above;

where B is -O-, -NH-, or -N(C<sub>1</sub>-C<sub>6</sub> alkyl)-;

where R<sub>C</sub> is: -(CH<sub>2</sub>)<sub>0-3</sub>-(C<sub>3</sub>-C<sub>7</sub>) cycloalkyl where cycloalkyl can be unsubstituted or substituted with one, two or three

(A) C<sub>1</sub>-C<sub>3</sub> alkyl unsubstituted or substituted with 1, 2, 3, or 4 -F,

-Cl, -Br, or -I,

(B) -CO-OH,

(C) -CO-O-(C<sub>1</sub>-C<sub>4</sub> alkyl),

(D) -OH, or

(E) C<sub>1</sub>-C<sub>6</sub> alkoxy,

or a pharmaceutically acceptable salt thereof.

Claim 50. (currently amended) The method of claim 49, wherein said compound inhibits 50% of β-secretase ~~the enzyme's~~ activity at a concentration of from about 0.1nM to about 200μM.

Claim 51. (currently amended) The method of claim 50, wherein said compound inhibits 50% of β-secretase ~~the enzyme's~~ activity at a concentration of from about 10nM to about 100μM.

Claim 52. (currently amended) The method of claim 51, wherein said compound inhibits 50% of β-secretase ~~the enzyme's~~ activity at a concentration of from about 100nM to about 50μM.

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Claim 53. (currently amended) The method of claim 52, wherein said compound inhibits 50% of  $\beta$ -secretase ~~the enzyme's~~ activity at a concentration of from about 1 $\mu$ M to about 10 $\mu$ M.

Claim 54. (previously presented) The method of claim 49, wherein said therapeutic amount is in the range of from about 0.1 to about 1000 mg/day.

Claim 55. (previously presented) The method of claim 49, wherein said therapeutic amount is in the range of from about 15 to about 1500 mg/day.

Claim 56. (previously presented) The method of claim 55, wherein said therapeutic amount is in the range of from about 1 to about 100 mg/day.

Claim 57. (previously presented) The method of claim 56, wherein said therapeutic amount is in the range of from about 5 to about 50 mg/day.

Claims 58-93 (cancelled)

Claim 94. (previously presented) A method according to claim 49, wherein the compound is

N-[(1*S*, 2*S*, 4*R*)-1-(3,5-Difluorobenzyl)-4-(*syn, syn*)-(3,5-dimethoxycyclohexylcarbamoyl)-2-hydroxyhexyl]-*N,N*-dipropylisophthalamide;

N-[4-(*R*)-(Cyclohexylmethyl-carbamoyl)-1-(*S*)-(3,5-difluorobenzyl)-2-(*S*)-hydroxy-hexyl]-*N,N*-dipropyl-isophthalamide;

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4-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-benzoylamino)-2-(*R*)-ethyl-4-(*S*)-hydroxy-hexanoylamino]-methyl)-cyclohexanecarboxylic acid methyl ester;

4-(*anti*)-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-benzoylamino)-2-(*R*)-ethyl-4-(*S*)-hydroxy-hexanoylamino]-methyl)-cyclohexanecarboxylic acid;

4-(*anti*)-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-benzoylamino)-4-(*S*)-hydroxy-2-(*R*)-methyl-hexanoylamino]-methyl)-cyclohexanecarboxylic acid;

4-(*anti*)-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-benzoylamino)-4-(*S*)-hydroxy-2-(*R*)-propyl-hexanoylamino]-methyl)-cyclohexanecarboxylic acid;

4-(*anti*)-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-benzoylamino)-4-(*S*)-hydroxyl-2-(*R*)-isobutyl-hexanoylamino]-methyl)-cyclohexanecarboxylic acid;

4-(*anti*)-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-benzoylamino)-4-(*S*)-hydroxy-hexanoylamino]-methyl)-cyclohexanecarboxylic acid;

4-(*anti*)-([2-(*R*)-Benzyl-6-(3,5-difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-benzoylamino)-4-(*S*)-hydroxy-hexanoylamino]-methyl)-cyclohexanecarboxylic acid;

4-(*anti*)-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-5-methyl-benzoylamino)-2-(*R*)-ethyl-4-(*S*)-hydroxy-hexanoylamino]-methyl)-cyclohexanecarboxylic acid;

4-(*anti*)-([6-(3,5-Difluoro-phenyl)-5-(*S*)-(3-dipropylcarbamoyl-5-methyl-benzoylamino)-2-(*R*)-ethyl-4-(*S*)-hydroxy-hexanoylamino]-methyl)-cyclohexanecarboxylic acid methyl ester;

4-(*anti*)-{[6-(3,5-Difluorophenyl)-5-(*S*)-(3-dipropylcarbamoylbenzoylamino)-2-(*R*)-ethyl-4-(*S*)-hydroxyhexanoylamino]-methyl}cyclohexanecarboxylic acid;

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N-[*(1S, 2S, 4R)*-1-(3,5-Difluorobenzyl)-4-(*syn,syn*)-(3,5-dimethoxycyclohexylcarbamoyl)-2-hydroxyhexyl]-*N,N*-dipropylisophthalamide; or

*N*-[4-(*R*)-(Adamantan-2-ylcarbamoyl)-1-(*S*)-(3,5-difluorobenzyl)-2-(*S*)-hydroxy-pentyl]-5-methyl-*N,N*-dipropyl-isophthalamide.

Claims 95-104. (cancelled)